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ning of each regular issue of the PCT Gazette.*

(54) Title: **USE OF A PROTEASOME INHIBITOR IN THE TREATMENT OF ENDOTHELIAL DYSFUNCTION AND/OR IN  
A LOW-DOSE PROTEASOME INHIBITOR THERAPY**

(57) Abstract: The present invention relates to the use of a proteasome inhibitor for the manufacture of a medicament for the pre-  
vention, onset therapy, acute therapy and/or regression of diseases associated with endothelial dysfunction. The present invention  
also relates to the use of a proteasome inhibitor as a low-dose treatment.

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/08495

## A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | WO 01/047540 A (BETH ISRAEL HOSPITAL)<br>5 July 2001 (2001-07-05)<br>*cf. abstract, page 7, lines 19-25, page 8, line 23 bridging with page 9, line 24, experiment 2 on pp. 46/47, claims 1/4/5*  | 1-10,<br>13-24        |
| X          | WO 99/09006 A (BEHNKE MARK ;ROUSH WILLIAM (US); PLAMONDON LOUIS (US); SOUCY FRANC)<br>25 February 1999 (1999-02-25)<br>*cf. abstract, page 9, line 15 bridging with page 10, line 2, page 31, line 2, page 41, lines 3-9, example 15 on page 67ff., page 69, lines 1-5, claims 71/72* | 1-10,<br>13-24        |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10, 13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

a) naturally occurring proteasome inhibitors comprising peptide derivatives which have a C-terminal epoxy keton structure, beta-lacton-derivatives, aclacinomycin A, lactacystin, clastolactacystin.

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2. claims: 1-10, 13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

b) synthetic proteasome inhibitors comprising: modified peptide aldehydes such as N-carbobenzoxy-L-leuciny-L-leuciny-L-leucinal (MG132), or the boric acid derivative of MG232, N-carbobenzoxy-Leu-Nva-H (MG115), N-acetyl-L-leuciny-L-leuciny-L-norleucinal (LLnL), N-carbobenzoxy-Ile-Glu(OBut)-Ala-Leu-H (PS1).

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3. claims: 1-10,13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

c) peptides comprising: an alpha,beta-epoxyketone-structure, vinyl-sulfones such as carbobenzoxy-L-leuciny-L-leuciny-L-leucin-vinyl-sulfon or 4-hydroxy-5-iodo-3-nitrophenylacetyl-L-leuciny-L-leuciny-L-leucin-vinyl-sulfon (NLVS).

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4. claims: 1-10, 13-24 (PART)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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